

We claim:

1. A method of processing blood, comprising the steps of:

5 removing blood from a subject for a removal time at a removal flow rate, thereby generating removed blood;

processing said removed blood, thereby generating processed blood including at least one return component;

10 returning at least a portion of said return component to said subject over a return time at a return flow rate; and

systematically varying said return flow rate over said return time.

15 2. The method of claim 1 wherein said return flow rate decreases over said return time.

3. The method of claim 1 wherein said return flow rate decreases in a substantially linear manner over said return time.

20 4. The method of claim 3 wherein said return flow rate is provided by the expression:

$$Z_{\text{ret}} = [F_0 + 2(1 - F_0)(t/t_r)] Q_{\text{ret}};$$

25 wherein  $Z_{\text{ret}}$  is said return flow rate,  $t$  is time,  $F_0$  has a value greater than 1 and less than or equal to 2,  $t_r$  is said return time and  $Q_{\text{ret}}$  is an average return flow rate.

5. The method of claim 4 wherein  $Q_{\text{ret}}$  is selected such that the extent of hemolysis during blood processing is less than about 0.1%.

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6. The method of claim 4 wherein  $Q_{ret}$  is a value selected from the range of about 50 ml min.<sup>-1</sup> and about 400 ml min.<sup>-1</sup>.

5 7. The method of claim 4 wherein  $t_r$  is a value selected from the range of about 0.5 min to about 0.9 min.

8. The method of claim 1 wherein said return flow rate decreases exponentially over said return time.

10 9. The method of claim 1 wherein said return flow rate decreases in a substantially exponential manner over said return time.

10. The method of claim 1 wherein said return flow rate increases over said return time.

15 11. The method of claim 1, further comprising the step of systematically varying said removal flow rate over said blood removal time.

12. The method of claim 1 wherein said removed blood is removed through a needle and said return component is returned through said needle.

20 13. The method of claim 1 wherein said removed blood is removed through a first access needle and said return component is returned through a second access needle.

14. The method of claim 1 wherein said processing step comprises the steps of:

25 separating said removed blood into a plurality of separated blood components including at least one collect component and said return component; and

collecting a collect component.

15. The method of claim 14 wherein said separating step comprises conducting said removed blood through a density centrifuge system.

16. The method of claim 14 wherein said separating step comprises conducting said removed blood through a centrifugal elutriation system.

17. The method of claim 14 wherein said collect component is plasma.

18. The method of claim 14 wherein said collect component is red blood cells.

19. The method of claim 14 wherein said collect component is white blood cells.

20. The method of claim 14 wherein said collect component is platelets.

21. The method of claim 1 wherein said blood is removed during a draw cycle and said portion of said return component is returned during a return cycle.

22. The method of claim 21 further comprising the step of sequentially repeating said draw and return cycles for a selected blood processing time.

23. A method of minimizing the incidence of an access blood vessel infiltration during blood processing, comprising the steps of:

removing blood from a subject for a removal time at a removal flow rate, thereby generating removed blood;

processing said removed blood, thereby generating processed blood including at least one return component;

returning at least a portion of said return component to said subject over a return time at a return flow rate, wherein said return flow rate decreases systematically during said return time.

24. A method of processing blood, comprising the steps of:

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removing blood from a subject for a draw cycle at a removal flow rate, thereby generating removed blood;

processing said removed blood, thereby generating processed blood including at least one  
10 return component; and

returning at least a portion of said return component to said subject.

sequentially repeating said draw cycle and return cycle for a selected blood processing  
15 time, whereby the removal flow rate is increased each draw cycle by a selected flow adjustment increment.

25. A method of processing blood, comprising the steps of:

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determining the total blood volume of a subject undergoing a blood processing procedure;

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removing blood from said subject at a selected removal flow rate thereby generating removed blood, wherein said selected removal flow rate is derived from said total blood volume;

processing said removed blood, thereby generating processed blood including at least one  
return component; and

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returning at least a portion of said return component to said subject at a return flow rate.

26. A method of processing blood, comprising the steps of:

determining the total blood volume of a subject undergoing a blood processing procedure;

removing blood from said subject, thereby generating removed blood;

processing said removed blood, thereby generating processed blood including at least one return component; and

returning at least a portion of said return component to said subject at a selected return flow rate, wherein said selected return flow rate is derived from said total blood volume of said subject.

27. A method of processing blood, comprising the steps of:

determining the total blood volume of a subject undergoing a blood processing procedure;

removing blood from said subject at a selected removal flow rate thereby generating removed blood, wherein said selected removal flow rate is derived from said total blood volume;

processing said removed blood, thereby generating processed blood including at least one return component; and

returning at least a portion of said return component to said subject at a selected return flow rate, wherein said selected return flow rate is derived from said total blood volume of said subject.

28. The method of claim 27 wherein said return and removal flow rates are linearly correlated to said total blood volume of said subject.

29. The method of claim 28 wherein said return and removal flow rates increase with increasing total blood volume of said subject.

30. The method of claim 27 wherein said removal flow rate is provided by the expression:

$$Z_{\text{rem}} = (M_{\text{rem}}) \times (V_B) \leq Q_{\text{rem max}},$$

wherein  $Z_{\text{rem}}$  is the removal flow rate,  $M_{\text{rem}}$  is a removal flow rate slope,  $V_B$  is the total blood volume of said subject and  $Q_{\text{rem max}}$  is a maximum removal flow rate.

31. The method of claim 27 wherein said return flow rate is provided by the expression:

$$Z_{\text{ret}} = (M_{\text{ret}}) \times (V_B) \leq Q_{\text{ret max}}$$

wherein  $Z_{\text{ret}}$  is the return flow rate,  $M_{\text{ret}}$  is a return flow rate slope,  $V_B$  is the total blood volume of said subject, and  $Q_{\text{ret max}}$  is a maximum return flow rate

32. The method of claim 27 wherein said subject is a human male and said total blood volume is determined using the expression:

$$V_B = 604 + \left( 3.669 \times 10^{-4} \right) \left( L^3 \right) + (32.187)(W)$$

wherein  $L$  is the length of the subject in units of centimeters,  $W$  is the weight of the subject in units of kilograms and  $V_B$  is total blood volume in units of milliliters.

33. The method of claim 27 wherein said subject is a human female and said total blood volume is determined using the expression:

$$V_B = 183 + \left( 3.561 \times 10^{-4} \right) \left( L^3 \right) + (33.069)(W)$$

wherein  $L$  is the length of the subject in units of centimeters,  $W$  is the weight of the subject in units of kilograms and  $V_B$  is total blood volume in units of milliliters.

34. The method of claim 30 wherein  $M_{rem}$  is a value selected from the range of about 0.0066  $\text{min}^{-1}$  and about 0.05  $\text{min}^{-1}$  and  $Q_{rem \max}$  is a value selected from the range of about 100  $\text{ml min}^{-1}$  to about 160  $\text{ml min}^{-1}$ .

35. The method of claim 34 wherein  $Q_{rem \max}$  is about 142  $\text{ml min}^{-1}$ .

36. The method of claim 31 wherein  $M_{ret}$  is a value selected from the range of about 0.025  $\text{min}^{-1}$  and about 0.200  $\text{min}^{-1}$  and  $Q_{ret \max}$  is a value selected from the range of about 200  $\text{ml min}^{-1}$  and about 400  $\text{ml min}^{-1}$ .

37. The method of claim 36 wherein  $Q_{ret \max}$  is about 302  $\text{ml min}^{-1}$ .

38. The method of claim 30 wherein  $M_{rem}$  is provided by the expression:

$$M_{rem} = (C_{qr}) \times (A_{rem})$$

wherein  $C_{qr}$  is a selectably adjustable processing rate parameter,  $A_{rem}$  is a constant having a value selected from the range of about 0.01  $\text{min}^{-1}$  to about 0.05  $\text{min}^{-1}$  wherein the value of  $C_{qr}$  is selected to avoid the occurrence of infiltration of an access blood vessel of said subject.

39. The method of claim 31 wherein  $M_{ret}$  is provided by the expressions:

$$M_{ret} = (C_{qr}) \times (A_{ret}),$$

wherein  $C_{qr}$  is a selectably adjustable parameter,  $A_{ret}$  is a constant having a value selected from the range of about 0.05  $\text{min}^{-1}$  to about 0.20  $\text{min}^{-1}$ , and wherein the value of  $C_{qr}$  is selected to avoid discomfort of said subject.

40. The method of claim 27 wherein said removed blood is removed through an access needle and said return component is returned through said access needle.

41. The method of claim 27 wherein said removed blood is removed through a first access  
5 needle and said return component is returned through a second access needle.

42. The method of claim 27 wherein said blood is removed during a draw cycle and said portion of said return component is returned during a return cycle.

10 43. The method of claim 42 further comprising the step of sequentially repeating said draw and return cycles for a selected blood processing time.

44. The method of claim 27 wherein said processing step comprises the steps of:

15        separating said removed blood into a plurality of separated blood components including at least one collect component and said return component; and

              collecting a collect component.

20 45. The method of claim 44 wherein said separating step comprises conducting said removed blood through a density centrifuge system.

46. The method of claim 44 wherein said separating step comprises conducting said removed blood through a centrifugal elutriation system.

25 47. The method of claim 44 wherein said collect component is plasma.

48. The method of claim 44 wherein said collect component is red blood cells.

30 49. The method of claim 44 wherein said collect component is white blood cells.



50. The method of claim 44 wherein said collect component is platelets.

51. A method of processing blood, comprising the steps of:

- 5        removing blood from a subject during a draw cycle, thereby generating removed blood;
- conducting said removed blood through a blood separation system, thereby generating a plurality of separated blood components including at least one collect component;
- 10        collecting a first portion of said removed blood corresponding to a collect component;
- recirculating a second portion of said removed blood through said blood separation system; wherein said second portion corresponds to a recirculated component of said removed blood;
- 15        returning a third portion of said removed blood to said subject during a return cycle, wherein said third portion corresponds to a return portion of said removed component;
- wherein the fraction by volume of said removed blood comprising said collected component is selected to prevent contamination of said collect component with red blood cells.
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52. The method of claim 51 further comprising the step of sequentially repeating said draw and return cycles for a selected blood processing time.

25    53. The method of claim 51 further comprising the step of adding an anticoagulant agent to said removed blood.

54. The method of claim 51 wherein recirculation of said recirculated component maintains quasi-steady state flow conditions in said blood separation system.

55. The method of claim 54 wherein recirculation of said recirculated component maintains quasi-steady state flow conditions in said blood separation system constant to within 10%.

56. The method of claim 51 wherein said blood separation system comprises a density centrifuge operationally connected to a centrifugal elutriation system.

57. The method of claim 51 wherein said removed blood has a first hematocrit,  $H_{rem}$ , and said recirculated component has a second hematocrit,  $H_{recir}$ , and wherein the weighted average of the hematocrit of said removed blood and the hematocrit of said recirculated component is less than

10 or equal to 
$$1 - \left( \frac{H_{rem}}{H_{recir}} \right)$$

58. The method of claim 51 wherein the weighted average of the hematocrit of said removed blood and the hematocrit of said recirculated component is less than 70%.

15 59. The method of claim 51 wherein said removed blood and said recirculated component are conducted through said blood processing system at a first rate,  $R_1$ , during said return cycle and wherein said removed blood and said recirculated component are conducted through said blood processing system at a second rate,  $R_2$ , during said draw cycle, wherein said removed blood has a first hematocrit,  $H_{rem}$ , and said recirculated component has a second hematocrit,  $H_{recir}$ , wherein  
20  $t_{draw}$  is the duration of the draw cycle and  $t_{ret}$  is the duration of the return cycle, wherein the fraction by volume of said removed blood comprising said collected component,  $F_{cmax}$ , is provided by the equation:

$$F_{cmax} = \left( \left( \left[ A^2 + \frac{(1-b)}{(1-D)} \right]^{0.5} - A \right) \right),$$

25 wherein b is provided by the equation:

$$b = \frac{H_{rem}}{H_{recir}},$$

D is provided by the equation:

$$D = \frac{t_{draw}}{t_{draw} + t_{ret}},$$

5 A is provided by the equation:

$$A = \frac{\left( \frac{1}{1-D} \right) + \left( \frac{C_r}{D} \right)}{2},$$

and  $C_r$  is provided by the equation:

$$10 \quad C_r = \frac{R_{ret}}{R_{draw}}$$

60. The method of claim 59 wherein b is a value selected from the range of about 0.46 to about 0.85.

15 61. The method of claim 59 wherein D is a value selected from the range of about 0.60 to about 0.73.

62. The method of claim 59 wherein  $C_r$  is a value selected from the range of about 0.4 to about 0.6.

63. The method of claim 51 wherein said collect component is platelets.

64. The method of claim 51 wherein said collect component is plasma.

65. The method of claim 51 wherein said collect component is white blood cells.

66. The method of claim 51 wherein said collect component is white blood cells and platelets.

67. The method of claim 51 wherein said removed blood is removed through an access needle and said return component is returned through said access needle.

68. The method of claim 51 wherein said removed blood and said recirculated component are conducted through said blood processing system at a first rate,  $R_1$ , during said return cycle and wherein said removed blood and said recirculated component are conducted through said blood processing system at a second rate,  $R_2$ , during said draw cycle, wherein said removed blood has a first hematocrit,  $H_{rem}$ , and said recirculated component has a second hematocrit,  $H_{recir}$ , wherein  $t_{draw}$  is the duration of the draw cycle and  $t_{ret}$  is the duration of the return cycle, wherein  $V_{svr}$  is the volume of removed blood required to fill a fixed volume return reservoir and  $V_{svnr}$  is the volume of the recirculated component recirculated each draw and return cycle, wherein the fraction by volume of said removed blood comprising said collected component,  $F_{cmax}$ , is provided by the equation:

$$F_{cmax} = \left( \frac{\left( \left[ A^2 + \frac{(1-z)(1-b)}{(1-D)} \right]^{0.5} - A \right)}{(1-z)} \right),$$

wherein  $b$  is provided by the equation:

$$b = \frac{H_{rem}}{H_{recir}},$$

$D$  is provided by the equation:

$$D = \frac{t_{draw}}{(t_{draw} + t_{ret})},$$

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$A$  is provided by the equation:

$$A = \left( \frac{\left( \frac{1}{1-D} \right) + \left( \frac{C_r}{D} \right)}{2} \right),$$

$C_r$  is provided by the equation:

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$$C_r = \left( \frac{R_{ret}}{R_{draw}} \right), \text{ and}$$

z is provided by the equation

$$z = \left( \frac{V_{svnr}}{V_{svn}} \right).$$